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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/675,020	09/29/2003	Stephen Donovan	17510DIV1 (BOT)	4829

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/675,020	DONOVAN, STEPHEN	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-21 and 36-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-21 and 36-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. This Action is responsive to Applicants amendment and remarks filed June 16, 2005. Claims 1-15 and 22-35 have been cancelled. Claims 36-44 have been added.

2. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

Rejection Maintained

3. The rejection under 35 U.S.C. 102(e) as anticipated by Yuzhakov et al is maintained for claims 16-21 and newly submitted claims 39 and 44 for the reasons set forth on pages 2-3, paragraph 2 of the previous Office Action.

The rejection was on the grounds that Yuzhakov et al teach a transdermal patch (columns 3-4) comprising a pharmaceutical composition which comprises a botulinum (column 51, lines 56-63), an enhancing agent (polymers) (column 28) and an adhesive to hold the patch in place (column columns 46 -47). Yuzhakov et al teach that the transdermal patch contains a microneedle array (column 3). Yuzhakov et al teach that the invention is projected or penetrates the stratum corneum column 3). Yuzhakov et al that Claims limitations such as "wherein the botulinum toxin is provided in a depot in the patch so that pressure applied to the patch causes botulinum toxin to be directed through the needles and under the stratum corneum" and "...wherein the botulinum toxin is provided in a dry state in a plurality of wells, each of the wells covered by a membrane that is dissolvable with a fluid, and wherein the enhancing agent mixes with the botulinum toxin as the membrane over a well dissolves so that the absorption of the botulinum toxin is enhanced would be inherent in the teaching of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's transdermal patch with the transdermal patch of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the transdermal patch of the prior art does not possess the same material structural and functional characteristics of the claimed transdermal patch). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that Yuzhakov et al do not teach each and every element of the claimed invention. Applicant urges that Yuzhakov et al do not teach a transdermal patch comprising an enhancing agent. Applicant urges that polymers are not employed as enhancing agents in Yuzhakov et al. Applicant urges that the prior art reference relies on voltage differentials to achieve drug delivery. Applicant urges that the prior art reference cannot anticipate the claims.

Applicant's arguments filed June 16, 2005 have been fully considered but they are not persuasive. It is the Examiner's position that the prior art reference anticipates the claimed invention. Yuzhakov et al teach a transdermal patch comprising a pharmaceutical composition which comprises a botulinum toxin and an enhancing agent (polymers). Although, Yuzhakov et al teach that polymers can be used to construct the closed-looped system used in the invention of the prior art, Yuzhakov et al also teach that porous polymers such as hydrogel or solgel matrix can be impreganated with active material to provide additional delivery mechanism (column 6). Therefore, one of ordinary skill in the art could reasonably concluded that polymers are used in the invention of the prior art as enhancing agents to aid with delivery of active materials. It should be noted that the instant specification includes polymers as one of the enhancing agents used in the claimed invention (see page 16 of the instant

specification). To address newly submitted claim 39, the prior art teaches that the enhancing agent provide additional delivery mechanism (column 6). Therefore the claim limitation "...facilitates transdermal administration of the botulinum toxin in a bioactive form to a subdermal target site of a human patient is taught in the prior art. Yuzhakov et al teach that double-sided tape (or double-stick tape) 1604 is used to temporarily hold in place the microneedle patch apparatus 1600 on the skin during its operation as well as to hold a thin layer of protective film 1602 (columns 46-47). Therefore, the claim limitation "...an adhesive disposed on one side of the transdermal patch to removably secure the patch on the patient's skin is taught in the prior art. Therefore, the prior art reference teaches the claimed invention.

New Ground of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 16-21 and newly submitted claims 36-44 are rejected under 35 U.S.C. 103(a) as unpatentable over Yuzhakov et al *(U.S. Patent No. 6,565, 532 B1 published May 20, 2003)* in view of Cevc *(U.S. Patent No. 6, 165, 500 published December 26, 2000).*

Claims 16-21 and 36-44 are drawn to a transdermal patch comprising a pharmaceutical composition which comprises a stabilized botulinum toxin, an enhancing agent and an adhesive.

Yuzhakov et al teach microneedle array structure (Abstract and claim 20, column 56). Yuzhakov et al teach that the microneedle array may be contained in a transdermal patch (columns 3-4). Yuzhakov et al teach that botulinum toxin can be delivery through the microneedle array. Yuzhakov et al teach a transdermal patch (columns 3-4) comprising a pharmaceutical composition which comprises a botulinum (column 51, lines 56-63) and an enhancing agent (polymers) (column 6).

Yuzhakov et al do not teach a transdermal patch wherein the enhancing agent is ethanol or comprises transfersomes.

Cevc teaches that solvents such as ethanol (enhancing agents) can be used to induce or increase the carrier system's capacity to form edges, protrusions or relatively strongly curved surfaces; this property also manifests itself in the capability to induce pores in lipid structures, such as membranes, or even provoke a solubilization (lysis) in the higher concentrations ranges (columns 7-8). Cevc teaches that the transfersome compositions of the invention can be introduced not only to a permeability barrier such as the skin (column 4, 66-67 and column 5, lines 1-4). Cevc teaches compositions that comprise transfersomes ranging in concentration from 0.1 to 99% of the total composition (column 4, lines 47-56). Therefore, the claim limitations "wherein the enhancing agent comprises, 1 part water, 1 part ethanol and 1 part polyethylene glycol " and "wherein the enhancing agent comprises 1 part of 10% and 0.9 part of a buffer"

are taught by the prior art. Cevc teaches that the ethanol use is absolute ethanol (columns 55-56), therefore the ethanol taught by the prior art teaches the claim limitation "wherein the ethanol is 90% ethanol".

It would be *prima facie* obvious at the time the invention was made to incorporate the transfersomes as taught by Cevc into the transdermal patches of Yuzhakov et al because Cevc teaches that the transfersome compositions can be introduced to a permeability barrier such as the skin and can also be transported into deeper tissues when they become systemically active. It would be expected barring evidence to the contrary, that incorporating transfersomes into transdermal patches would be an effective way to facilitate the delivery of active agents such as botulinum toxin to a subdermal target of a patient.

Status of Claims

5. No claims allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
August 31, 2005

L. R. F. Smith
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